REMARKS/ARGUMENTS

THE INVENTION

This invention provides for novel peptide analogs that are agonists of CXCR4.

STATUS OF THE CLAIMS

Claims 1-32 are canceled. New claims 33-35 are pending.

New claim 33 presents the amino and carboxy peptides of the composition of previously pending claim 32 and recites conventional preamble language for novel compositions and a pharmaceutically acceptable carrier which is supported on page 20, lines 1-14 of the specification. The definition for the linker finds support at page 44, lines 20-23, defining L_n as a linker with an n of 1-50, lines 26-28 reciting alkyls of less than 20, and glycines of 3 to 4 at page 47, lines 21-22.

SUBSTITUTE SEQUENCE LISTING AND AMENDMENTS

A thorough review of the Specification was undertaken to assign the proper sequence identifiers to the sequences found in the new claims. The Substitute Sequence Listing is submitted herewith to enter sequences inadvertently omitted from the Sequence Listing submitted September 9, 2002.

Entry into the Substitute Sequence Listing of structures containing the non-peptide linker moiety $-(CH_2)_n-$, where n = 0-20), was accomplished by providing two separate peptide sequences where one SEQ ID NO: contained a modified terminal amino acid described as substituted by the linker and further modified by another SEQ ID NO:. The second SEQ ID NO: described a modified terminal amino acid including the linker further modified by the first SEQ ID NO:.

The amendment to the paragraph beginning on page 46, line 12, amended two sequences where double underlining indicated linked residues. On page 45, lines 2-5 define the double underlining as indicating residues joined by side chain cyclization. The sequences amended show three such residues, where the accompanying formulae ("SDF-1(1-14)-$(G)_4$-SDF-1(55-67)-

K20/D24-cyclic acid" and "SDF-1(1-14)-$(G)_4$-SDF-1(55-67)-K20/D24-cyclic amide", respectively) indicate that the residues involved in cyclization were intended to be only "K20/D24". The double underlining for the "K" at position 28 has, therefore, been removed.

In three cases, *i.e.*, page 60, line 17; page 61, line 26; and page 75, line 45, the peptide "CTCE-0021" or "CTCE0022-like" structures have been described as a "cyclic acid", where their accompanying formulae expressly indicate a carboxy-terminal amide (-$CONH_2$) group. Further, page 50, lines 36-40 and page 53, lines 21-22, clearly indicate that both compounds should be labeled as "cyclic amide."

The amendments to the "CTCE-0021-like Analogs" on pages 62-68 and the "CTCE-0022-like Analogs" on pages 68-74, insert sequence identifiers for only those peptides which do not contain obligate D-amino acid residues. This is in conformity with 37 C.F.R. § 1.821(a)(2), which states "Those amino acid sequences containing D-amino acids are not intended to be embraced by this definition." This is in contrast to sequences containing optional L- or D-amino acids, such as those on page 16, lines 27-32, for example, where an "Xaa" residue was defined as "an amino acid that may...be either an L-Proline or a D-Proline moiety", which were included in the Substitute Sequence Listing.

The amended sequence on page 75, line 46-47, "Structure of CTCE0021", has the bracket indicating the position of the cyclized residues moved to conform to the "K20/E24" description on line 45.

Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-214, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk.

The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy. This amendment contains no new matter.

INTERVIEW

Pursuant to Rule 133(b), applicants acknowledge with appreciation the telephonic interview on May 27, 2006. During the interview, the scope of the claims was discussed and applicants agreed to limit the claims to the specific sequences identified in a presently presented claim. While no agreement on language was agreed upon, the Examiner did not object to considering claims reciting a genus of linkers.

TIMELINESS OF THE AMENDMENTS

The proposed amendments are appropriate for consideration after a final Office Action. The amendments limit the scope of the claims to the peptides recited in claim 32 (now canceled) and therefore reduce the issues for appeal. No new matter is introduced and no additional searches are required as the amendments to the claims were already examined when claim 32 was considered.

The amendments to comply with Rule 1.821 were introduced as soon as they were discovered and were not responsive to a USPTO request.

OBJECTIONS

Claim 28 was objected to because it depended from canceled claims. Claim 28 has been canceled.

REJECTIONS

There are no prior art rejections. The primary basis for rejecting the claims is for lack of enablement and description. There is a new matter rejection which has been addressed by amendment.

A. ENABLEMENT

The Examiner believed that the scope of the previously pending claims remained overly broad and that it would take undue experimentation to generate and test all the species included in the claims.

The Examiner wrote on page 4 of the outstanding Office Action:

> Undue experimentation would be required of one skilled in the art to generate the infinite number of CXCR4 peptides recited in the claims and screen the same for activity. Although the Applicant has amended claim 23, the claims are still interpreted by the Examiner as encompassing a large number of CXCR4 agonist peptides.

In response, applicants have restricted the claim scope to the N and C termini of a preferred species.

The claims now recite a family of active pharmaceutical compounds that differ by an inert linking group. The active components are set forth with specificity. Applicants believe that this amendment fully addresses the Examiners' outstanding concerns.

Let us now turn to the Examiner's specific concerns.

1. The specification does not teach the generation and screening of any other agonists.

On page 5 of the final Office Action the examiner states that "the specification does not teach the generation and screening of any other agonists" except for the species listed in the action. In view of the amendments, applicants submit that this issue is no longer a valid concern. Unless the Examiner has an objective reason for why the linker plays a critical role in the binding of the compositions to CXCR4, the claimed species should be enabled.

2. There is little guidance in the specification.

The Examiner is concerned that there is little guidance in the specification indicating which amino acids from the N-terminal domain and which amino acids from the C-terminal

domain can be linked together to generate a functional agonist peptide. As amended, the claims now dictate with exact precision residues that generate a functional peptide.

3. One of skill in the art would not be able to predict the structure and function of the CXCR4 peptide when the peptide contains a spacer containing one to three glycine residues.

The Examiner is concerned that "a large quantity of experimentation" would be required to generate and screen agonist with a variety of spacers (page 5 of the Office Action). The Examiner is reminded that "quantity of experimentation" required to practice an invention is not the proper legal test for enablement. The true test is whether that work constitutes undue experimentation.

Here the Examiner has not provided any objective evidence or reasoning as to why the spacer might be a critical feature of the invention. If it were critical, and if it required significant experimentation to identify operable embodiments, the Examiner's concerns would be well taken. However, the spacer region is not critical to function beyond its ability to provide flexibility. The Examiner relies on Luo et al. But the Lou reference merely states the need for *flexibility* at this point in the molecule. Applicants comply with this requirement by reciting a linker. However, the linker is a spacer that serves no biological function other than to assist in the positioning of the two peptide domains. The spacer can be carbon atoms, as in a methylene bridge of 1 to twenty carbons, or a bridge made of carbons, nitrogens and oxygens of from 5 to 20 atoms (Gly_{1-4}).

Having amended the claims to address the claim scope issue, and having addressed the Examiner's specific concerns regarding enablement, applicants submit that the enablement rejection has been fully addressed. Unless the Examiner has some objective reason to rebut the above remarks, the enablement-based rejections should be withdrawn.

B. DESCRIPTION

The Examiner finds the previously pending claims to lack description because the applicants did not possess all the species encompassed by the claims. As amended, the claims

now recite a scope of structure that fully meets the description requirement. More specifically, the problematic language "homologous" has been deleted, and precise sequences are now recited for the amino and carboxy termini. This language, coupled with the recitation a precise family of linkers now limits the claimed species to a reasonable number, and this fully addresses the argument of lack of possession. In view of the amendments, there is no longer a legal basis to maintain the description rejection and applicants respectfully request that this basis for the rejection be withdrawn.

C. NEW MATTER

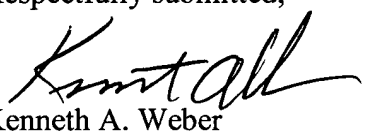
The Examiner noted that there was no support for an alkyl chain of 1-4. As amended, the claims now recite an alkyl chain of 1-20 for which support is found in the specification as recited above.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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